IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

AUG 0 8 2001

Atty. Docket No: 065691/0222

The patent application of

CHAMBON, PIERRE et al.

Serial No. 09/853,033

Filed: May 11, 2001

For: TRANSGENIC MOUSE FOR TARGETED RECOMBINATION MEDIATED

BY MODIFIED CRE-ER

STATEMENT TO SUPPORT FILING AND SUBMISSION IN ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Assistant Commissioner for Patents Washington, D.C. 20231
Box SEQUENCE

Sir:

In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

- 1. the submission, filed herewith in accordance with 37 C.F.R. § 1.821(g), does not include new matter;
- 2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same; and
- 3. all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

James A. Coburn

HARBOR CONSULTING

Intellectual Property Services 1500A Lafayette Road Suite 262 Portsmouth, N.H. 800-318-3021



SEQUENCE LISTING

<110> METZGER, DANIEL

<120> TRANSGENIC MOUSE FOR TARGETED RECOMBINATION MEDIATED BY MODIFIED CRE-ER

<130> 065691/0222

<140> 09/853,033

<141> 2001-05-11

<150> FR 00/12570

<151> 2000-10-03

<160> 14

<170> PatentIn Ver. 2.1

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<211> 1788

<212> DNA

<213> Homo sapiens

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<221> CDS

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ccc gcc gtg tac aac tac ccc gag ggc gcc gcc tac gag ttc aac gcc 192 Pro Ala Val Tyr Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala 50

gcg gcc gcc aac gcg cag gtc tac ggt cag acc ggc ctc ccc tac 240 Ala Ala Ala Asn Ala Gln Val Tyr Gly Gln Thr Gly Leu Pro Tyr 65

ggc ccc ggg tct gag gct gcg gcg ttc ggc tcc aac ggc ctg ggg ggt 288 Gly Pro Gly Ser Glu Ala Ala Phe Gly Ser Asn Gly Leu Gly Gly 85

ttc ccc cca ctc aac agc gtg tct ccg agc ccg ctg atg cta ctg cac 336 Phe Pro Pro Leu Asn Ser Val Ser Pro Ser Pro Leu Met Leu Leu His 100 105

· •

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	ccg Pro		_							_		_	_	_		480
	aga Arg	_	_	_	_	_			_	_		_		_	_	528
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	ggc Gly					_			_			_	_	-		624
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	cag Gln				_					_	-	_	_	_	_	720
	ctc Leu															768
	gac Asp	_	_			_	_	_			_	_	_	_	_	816
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_	aac Asn 290					_		_			_		_	_		912
	ctg Leu															960
_	gct Ala										_			_		1008

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	atc Ile														1488
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	atc Ile														1584
	tgc Cys 530														1632
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200

205

Phe Lys Arg Ser Ile Gln Gly His Asn Asp Tyr Met Cys Pro Ala Thr 210 Asn Gln Cys Thr Ile Asp Lys Asn Arg Arg Lys Ser Cys Gln Ala Cys 230 235 Arg Leu Arg Lys Cys Tyr Glu Val Gly Met Met Lys Gly Gly Ile Arg 250 Lys Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Met Arg Ala 280 Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn 290 Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu 310 315 Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro 325 Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg 345 Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu 375 Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Gly 385 390 Lys Leu Leu Phe Ala Pro Asn Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser 420 Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu

Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser 450 460

Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp 465 470 475 480

Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr 485 490 495

Leu Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser 500 505 510

His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met 520 515 Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Glu Met Leu 535 Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser Val 550 555 Glu Glu Thr Asp Gln Ser His Leu Ala Thr Ala Gly Ser Thr Ser Ser 565 570 His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe Pro Ala Thr Val 595 <210> 3 <211> 1983 <212> DNA <213> Artificial sequence <220> <221> CDS <222> (1)..(1983) <220> <223> Description of Artificial Sequence: Chimeric sequence Homosapiens-Bacteriophage P1 <400> 3 atg tcc aat tta ctg acc gta cac caa aat ttg cct gca tta ccg gtc 48 Met Ser Asn Leu Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val 10 gat gca acg agt gat gag gtt cgc aag aac ctg atg gac atg ttc agg Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg gat cgc cag gcg ttt tct gag cat acc tgg aaa atg ctt ctg tcc gtt 144 Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val tgc cgg tcg tgg gcg gca tgg tgc aag ttg aat aac cgg aaa tgg ttt 192 Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe ccc gca gaa cct gaa gat gtt cgc gat tat ctt cta tat ctt cag gcg 240 Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala cgc ggt ctg gca gta aaa act atc cag caa cat ttg ggc cag cta aac 288 Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn 85 90

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				atg Met												384
_		-		cag Gln	_				_	_		_		_	_	432
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				att Ile										_		624
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	aac Asn									1008
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	gct Ala									1200
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	 ctg Leu	_								1296
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	tct Ser 515		_					_		1584
	Leu								ctg Leu	1632

_	aag Lys					_			_	_	_	_	_		_	1680
	ctg Leu															1728
	cac His				_	_			_	-	-		_		_	1776
	aag Lys									_	_	_	_		_	1824
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1				5					10					15		
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Asp	Arg	Gln 35	Ala	Phe	Ser	Glu	His 40	Thr	Trp	Lys	Met	Leu 45	Leu	Ser	Val	
Cys	Arg 50	Ser	Trp	Ala	Ala	Trp 55	Cys	Lys	Leu	Asn	Asn 60	Arg	Lys	Trp	Phe	
Pro 65	Ala	Glu	Pro	Glu	Asp 70	Val	Arg	Asp	Tyr	Leu 75	Leu	Tyr	Leu	Gln	Ala 80	

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- Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110
- Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly
 115 120 125
- Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln 130 135 140
- Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu 165 170 175
- Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg
 180 185 190
- Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly
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- Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp 210 215 220
- Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 225 230 235 240
- Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu 245 250 255
- Ser Thr Arg Ala Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile 260 265 270
- Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 275 280 285
- His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 290 295 300
- Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 305 310 315 320
- Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 335
- Arg Leu Leu Glu Asp Gly Asp Leu Glu Pro Ser Ala Gly Asp Met Arg 340 345 350
- Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys 355 360 365
- Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu 370 375 380

Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg 385 390 395 400

Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp 405 410 415

Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe 420 425 430

Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp
435
440
445

Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro 450 455 460

Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly
465 470 475 480

Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr \$485\$

Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys 500 505 510

Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser 515 520 525

Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu 530 535 540

Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu 545 550 555 560

Thr Leu Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu 565 570 575

Ser His Ile Arg His Met Ser Asn Lys Arg Met Glu His Leu Tyr Ser 580 590

Met Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Glu Met 595 600 605

Leu Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser 610 615 620

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Pro Ala Thr Val 660

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<212> DNA

<213> Artificial sequence

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				gat Asp												96
				ttt Phe												144
				gcg Ala												192
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				cgg Arg												336
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				cag Gln												432
_	_			atg Met	_		_	_	_	_	_	_		_		480
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_											acc Thr			624
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											ctg Leu			720
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											cga Arg 270			816
		_	_	_				_			tgg Trp			864
											gct Ala			912
					_						gta Val			960
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_	_										tct Ser			1104
											agt Ser		ttg Leu	1152
											cct Pro			1200
											ctg Leu			1248

agg gag Arg Glu		al His	_		Asn			_						1296
gtg gat Val Asp	_		_	Asp	_	_				_	_	_		1344
cta gag Leu Glu 450		_	Ile C			_		_		_				1392
gtg aag Val Lys 465		_	_			_		_	_			_		1440
aaa tgt Lys Cys														1488
tca tct Ser Ser		ne Arg												1536
ctc aaa Leu Lys				Leu										1584
agc acc Ser Thr 530	Leu Ly	-	Leu (-		_	-				_	_	_	1632
gac aag Asp Lys 545		-		-						_	-		_	1680
acc ctg Thr Leu														1728
tcc cac Ser His	Ile Ar													1776
atg aag Met Lys				Val										1824
gcg gac Ala Asp 610	Ala Hi		Leu 1											1872
gtg gag Val Glu 625				_		_	_							1920

1983

tcg cat tcc ttg caa aag tat tac atc acg ggg gag gca gag ggt ttc 1968 Ser His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe 645 650 655

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<212> PRT

<213> Artificial sequence

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<223> Description of Artificial Sequence: Chimeric sequence Homosapiens-Bacteriophage P1

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Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg 20 25 30

Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 40 45

Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 50 55 60

Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 65 70 75 80

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn 85 90 95

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110

Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly
115 120 125

Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln 130 135 140

Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn 145 150 155 160

Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu 165 170 175

Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg
180 185 190

Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly
195 200 205

Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp 210 215 220

Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 225 230 235 240

Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu 245 250 255

Ser Thr Arg Ala Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile
260 265 270

Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 275 280 285

His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 290 295 300

Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 305 310 315 320

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 335

Arg Leu Leu Glu Asp Gly Asp Leu Glu Pro Ser Ala Gly Asp Met Arg 340 345 350

Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys 355 360 365

Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu 370 375 380

Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg 385 390 395 400

Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp \$405\$

Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe 420 425 430

Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp 435 440 445

Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro 450 455 460

Val Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly 465 470 475 480

Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr 485 490 495

Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys 500 505 510

Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser 515 Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu 535 Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu 550 555 Thr Leu Gln Gln His Gln Arg Leu Ala Gln Leu Leu Ile Leu 565 Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Glu Ala Ala Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser 615 Val Glu Glu Thr Asp Gln Ser His Leu Ala Thr Ala Gly Ser Thr Ser 625 630 Ser His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe 650 Pro Ala Thr Ala 660 <210> 7 <211> 1983 <212> DNA <213> Artificial sequence <220> <221> CDS <222> (1)..(1983) <220> <223> Description of Artificial Sequence: Chimeric sequence Homosapiens-Bacteriophage P1 <400> 7 atg tcc aat tta ctg acc gta cac caa aat ttg cct gca tta ccg gtc 48 Met Ser Asn Leu Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val gat gca acg agt gat gag gtt cgc aag aac ctg atg gac atg ttc agg 96 Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg gat cgc cag gcg ttt tct gag cat acc tgg aaa atg ctt ctg tcc gtt 144 Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 40

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		gaa Glu														240
		ctg Leu														288
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		ctg Leu 115														384
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		tca Ser														480
		ttt Phe														528
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atg Met	tta Leu	atc Ile 195	cat His	att Ile	ggc Gly	aga Arg	acg Thr 200	aaa Lys	acg Thr	ctg Leu	gtt Val	agc Ser 205	acc Thr	gca Ala	ggt Gly	624
		aag Lys														672
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		aga Arg														768
		cgc Arg		Leu					Glu					Leu		816

			_	gat Asp	_				_		-	_				864
				gtc Val												912
		_		atc Ile	_		-						_			960
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				gat Asp												1056
_	_			tgg Trp		_	_		_			_		_	-	1104
				ttg Leu												1152
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		_	_	gct Ala 405	_	_	_			_			_	_	_	1248
				cac His												1296
				ctc Leu												1344
				atg Met												1392
				ttt Phe												1440
	_	_		ggc Gly 485	_					_	_	_	_	_		1488

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	er											cga Arg		1632
A		_		_		_		_	_	_	_	gca Ala	 _	1680
												ctc Leu		1728
					_	_						ctg Leu 590		1776
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		_	gct Ala 660	tga										1983

<210> 8

<211> 660

<212> PRT

<213> Artificial sequence

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<223> Description of Artificial Sequence: Chimeric sequence Homosapiens-Bacteriophage P1

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Met Ser Asn Leu Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val 1 5 10 15

Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg 20 25 30

Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Ser Val 35 40 45

Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 50 55 60

Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 65 70 75 80

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn 85 90 95

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110

Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly 115 120 125

Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln 130 135 140

Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn 145 150 155 160

Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu 165 170 175

Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg
180 185 190

Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly 195 200 205

Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp 210 215 220

Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 225 230 235 240

Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu 245 250 255

Ser Thr Arg Ala Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile 260 265 270

Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 275 280 285

His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 290 295 300

Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 305 310 315 320 عاد الإيكام

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 335

Arg Leu Leu Glu Asp Gly Asp Leu Glu Pro Ser Ala Gly Asp Met Arg 340 345 350

Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys 355 360 365

Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu 370 375 380

Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg 385 390 395 400

Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp
405 410 415

Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe 420 425 430

Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp 435 440 445

Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro 450 455 460

Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly 465 470 475 480

Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr 485 490 495

Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys 500 505

Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser 515 520 525

Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu 530 535 540

Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu 545 550 555 560

Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Ile Leu
565 570 575

Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser 580 585 590

Met Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Glu Ala 595 600 605

Ala Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser 610 615 620

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